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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,047	07/22/2003	Claude F. Meares	023070-130910US	1090
43850 7590 05/11/2007 MORGAN, LEWIS & BOCKIUS LLP (SF) 2 PALO ALTO SQUARE 3000 El Camino Real, Suite 700 PALO ALTO, CA 94306			EXAMINER FETTEROLF, BRANDON J	
			ART UNIT 1642	PAPER NUMBER
			MAIL DATE 05/11/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/625,047	<b>Applicant(s)</b> MEARES ET AL.	
	<b>Examiner</b> Brandon J. Fetterolf, PhD	<b>Art Unit</b> 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 07 February 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,6-8,10-24,26,27,30,31 and 33-36 is/are pending in the application.
- 4a) Of the above claim(s) 16-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,6-8,10-15,24,26,27,30,31 and 33-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>5/09/2006</u> | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Response to the Amendment***

The Amendment filed on 02/07/2007 in response to the previous Non-Final Office Action (3/24/2006) is acknowledged and has been entered.

Claims 1, 6-8, 10-24, 26-27, 30-31 and 33-36 are currently pending.

Claims 16-23 have been withdrawn from consideration as being drawn to a non-elected invention.

Claims 1, 6-8, 10-15, 24, 26-27, 30-31 and 33-36 are under consideration.

### ***Information Disclosure Statement***

The Information Disclosure Statement filed on 5/09/2006 and the submission of the missing reference on 5/11/2006 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

### **Rejections Withdrawn:**

The rejection of Claims 1-4, 10-15 and 28-29 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn in view of Applicants arguments.

The rejection of Claims 1, 6-8, 10-15, 24 and 26-27 under 35 U.S.C. 112, first paragraph, enablement has been withdrawn in view of Applicants arguments.

### **Rejections Maintained:**

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6-8, 10-15, 24 and 26-27 **remain** rejected and **new** claims 30 and 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Hansen et al. (WO 99/66951).

Hansen et al. teach a method of treating diseased tissues in a patient, comprising: (a) administering to a patient a bi-specific antibody or antibody fragment having at least one arm that specifically binds to a targeted tissue and at least one arm that specifically binds a targetable conjugate; (b) optionally, administering to said patient a clearing composition, and allowing said composition to clear non-localized antibodies or antibody fragments from circulation; and (c) administering to said patient a first targetable conjugate which comprises a carrier portion which comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment, and one or more therapeutic agents (page 58, claim 1 of WO document). With regards to the targetable conjugate's epitope, the WO document teaches (page 9, lines 30-33) that the epitope includes, but is not limited to, a hapten. With regards to the hapten, Hansen et al. teach (page 10, line 2 and page 34, lines 27-28) that haptens include, but are not limited to, chelators such as DPTA and DOTA. For example, the WO document teaches (page 35, lines 7-11) a method of treating CEA-expressing tumors, wherein a bi-specific antibody with at least one arm, which specifically binds to CEA, and at least one arm, which specifically binds the targetable conjugate whose hapten is a conjugate of yttrium-DOTA is administered to a patient. With regards to the bi-specific antibody which recognizes CEA and a metal chelate such as DOTA, the WO document teaches (page 10, lines 26-33) that the bi-specific antibody is generated by derivatizing an anti-CEA F(ab')<sub>2</sub> mAB with a hydrazide-maleimide cross-linker and coupling said derivatized anti-CEA F(ab')<sub>2</sub> to an anti-chelate Fab'-SH. Moreover, Hansen et al. teach (page 24, lines 24-33) that chelators, such as DOTA, may be conjugated to the carrier portion of a targetable conjugate by generating a reactive functional group such as carbodiimide and coupling the carbodiimide to the peptides free amines. Thus, while Hansen et al. does not teach a macrocyclic metal chelate comprising four nitrogen atoms as shown in the formula of claim 6 or an S configuration DOTA, the referenced limitations are an inherent structural feature of DOTA as evidenced by Sigma-Aldrich (see attached document of record). Thus, the claimed antibody appears to recognize the same macrocyclic metal chelate as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that a product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the

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absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

In response to this rejection, Applicants assert that the instant rejection over Hansen, referred to herein as Hansen II, is similar to the Hansen reference (US 2002/0006379, 1/17/2002) cited in the previous Office Action. As in the first Hansen reference, the targetable conjugate in Hansen II is a DOTA chelate with a peptide side chain. As such, Applicants assert that while Hansen II's antibody recognizes a targetable conjugate, the antibody is only recognizing a peptide sequence on the conjugate, and not the macrocyclic metal chelate itself. Therefore, Applicants contend that Hansen II is missing Applicants' element of an antibody that "recognizes a macrocyclic metal chelate". Since all the elements of the Applicants' invention are not present in Hansen II, Applicants argue that the anticipation rejection cannot be maintained.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants' assertions that the targetable conjugate of Hansen II is a DOTA chelate with a peptide side chain, the Examiner acknowledges that there are instances in Hansen II which teach DOTA with a peptide side chain (see for example, page 34, lines 20-25). However, in this example the Examiner recognizes that the "peptide side chain" of the DOTA conjugate only appears to serve as a linker between the DOTA chelate and for example, a chemotherapeutic agent such as SN-38; and does not appear to be what is being recognized by the antibody as asserted by Applicants. Moreover, it is clear from the teachings of Hansen II, as noted above, that the hapten, in this case DOTA, serves as the "epitope" recognizable by said at least one other arm of said bi-specific antibody or antibody fragment. Lastly, assuming, *arguendo*, that the antibody is recognizing the peptide side chain of DOTA, the Examiner recognizes that this still does not appear to result in a manipulative difference between the claimed invention and the prior art since the claims are drawn to a macrocyclic chelate, wherein the macrocyclic chelate is substituted or unsubstituted DOTA. Thus, a DOTA chelate with a peptide side chain could reasonably encompass substituted DOTA. Therefore, claims 1, 7-8, 10-15, 24 and 26-27 **remain** rejected and **new** claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Hansen et al..

**New Rejections Necessitated by Amendment:**

### ***Claim Objections***

Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 6, which depends from independent claim 1, is drawn to a substituted or unsubstituted DOTA having a generic heterocyclic ring structure similar to DOTA when "d" is 1. However, the claims encompass "d" being 2 in addition to 1. As such, if "d" is 2, e.g., 11 carbons in the ring, then the structure would no longer be DOTA, substituted or unsubstituted because DOTA is a tetraazododecane ring structure, e.g., 10 carbons in the ring (see Sigma of record).

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 recites the limitation "said localizing" in the second line of claim 31. However, upon careful review of claim 31, as well as claim 1, from which claim 31 depends, there is insufficient antecedent basis for this limitation in the claim.

Therefore, NO claim is allowed

**All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.**

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

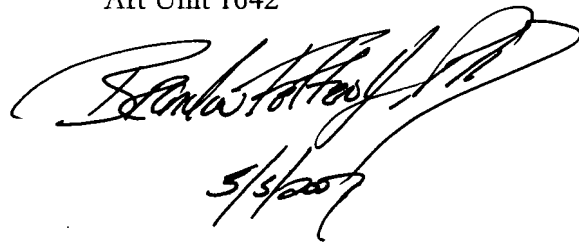
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner  
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5/5/2007



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